COMMENTS

Priority:

The Office Action states that there is no support in U.S. Provisional Application No. 60/463,629 for claims to a method of treating a neoplasm by administering a fibrate. Applicant believes it may be entitled to benefit of the '629 Provisional for the presently amended claims, but will defer addressing this issue until such time as one or more claims are deemed allowable over the prior art.

Drawings:

The Office Action states that the drawings are objected to as failing to comply with 37 C.F.R. 1.84(p)(5) because they contain reference characters not mentioned in the description. Applicants have amended the specification to describe these reference characters. The newly added descriptions are fully supported by the specification as originally filed, and as such do not add new matter.

Applicant has also submitted a corrected version of Figure 1 that contains the reference characters A and B, as set forth in paragraph 0054 of the application as originally filed.

Claim objections:

The Office Action states that claim 6 is objected to because the word "a" is missing between the words "with" and "fibrate." Applicants have amended claim 6 to include this missing word.

The Office Action states that claim 8 is objected to because the word "gemfibrizil" is misspelled. Applicants have amended claim 8 to correct this misspelling.

The Office Action states that claim 10 is objected to because "chemotherapeutics" should be singular. Applicants have amended claim 10 to correct this.

Rejections under 35 U.S.C. 112 (second paragraph):

The Office Action states that claims 6-10 are rejected as indefinite because claims 6 and 10 recite the limitation "comprising a step of." According to the Office Action, this limitation is indefinite because it is not clear if other steps are intended to follow. Applicants have removed the term "a step of" from claims 6 and 10, which the Office Action states is sufficient to overcome this rejection.

Rejections under 35 U.S.C. 112 (first paragraph):

The Office Action states that claims 6 and 9-10 are rejected for failing to comply with the written description requirement. As set forth in the Office Action, these claims are drawn to administration of a fibrate. According to the Office Action, the specification does not provide sufficient distinguishing identifying characteristics of the genus, and therefore does not provide adequate written description of the genus.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings,...*or* by disclosure of relevant, identifying characteristics. What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. M.P.E.P. 2163(II)(A)(3)(a)(ii).

As acknowledged in the Office Action at page 6, the specification discloses five specific examples of fibrates: clofibric acid, ciprofibrate, gemfibrozil, bezafibrate, and

fenofibrate. In addition, the specification provides the chemical structure of bezafibrate and clofibric acid and discloses experimental data showing that three different fibrates (bezafibrate, gemfibrozil, and clofibric acid) inhibit aldose reductase activity as presently claimed (see Example 20 and Table 1). The Office Action further acknowledges at page 11 that "Fibrates are well known in the art as lipoprotein lipase activators and hypolipidemic drugs." Given the high level of skill and knowledge in the art with regard to fibrates, the specification provides "sufficient description of a representative number of species by actual reduction to practice" to support the claimed genus.

Additionally, the term "fibrates" is a sufficient "relevant, identifying characteristic" in and of itself to describe the claimed genus. As set forth in the present application at page 15, "Fibrates are commonly known to be compounds that decrease serum triglyceride and increase HDL." Bezafibrate, ciprofibrate, gemfibrozil, and fenofibrate are currently marketed for use in the treatment of high cholesterol under the brand names Bezalip®, Modalim®, Lopid®, and TriCor®, respectively. Therefore, the skilled artisan would immediately recognize that the term "fibrate" as set forth in the specification has a well-known meaning and encompasses a specific set of compounds.

As cited at page 7 of the Office Action, the Federal Circuit stated in *Regents of Univ. of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1567 (Fed. Cir. 1997) that "[A] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] *chemical name*', of the claimed subject matter sufficient to distinguish it from other

materials" (emphasis added). The *Lilly* Court went on to state that "naming a type of material generally known to exist, in the absence of knowledge as to what the material consists of, is not a description of that material" (emphasis in Office Action). *Lilly* at 1568, quoted by the Office Action at page 11. In the present situation, the term "fibrate" is sufficiently well known in the art to function as a chemical name that distinguishes the claimed subject matter from other materials. There is no "absence of knowledge as to what the material consists of" because the term "fibrates" has a well known meaning in the art.

As further cited at page 7 of the Office Action, *Lilly* stated that the problem with the generic terminology in the claims was that "it does not distinguish the claimed genus from others, except by function." *Lilly* at 1568, cited by Office Action at page 11. The Court went on to state that "It is only a definition of a useful result rather than a definition of what achieves that result....The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made the invention." *Lilly* at 1568. Finally, *Lilly* stated "Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what the material consists of, is not a description of the material." *Id.*

The rationale of *Lilly* does not apply to the present claims, which do not attempt to distinguish the claimed genus based on function. This is not a situation where the claims recite "a type of material generally known to exist" without "knowledge as to what the material consists of." As stated above, the term "fibrates" is well known in the art to describe a specific set of chemical compounds, and is

sufficient to enable the skilled artisan to visualize and recognize the identity of the members of the genus.

The sufficiency of the term "fibrate" to describe the claimed genus is illustrated by the number of patents that have issued with generic fibrate claims. For example, U.S. Patent No. 6,133,293 claims a method for treating diabetic complications comprising administering "a therapeutically effective amount of an in insulin sensitivity enhancer in combination with a fibrate compound." The '293 Patent lists 15 specific examples of fibrates, but does not provide a structural description for the genus. Further, unlike the present specification, the '293 Patent does not provide experimental results for any fibrate. U.S. Patent No. 6,362,236 claims a method of inhibiting oxidation of lipoproteins by administering "a hydroxylated cholesterol lowering agent selected from a hydroxylated statin or a hydroxylated fibrate." The '236 Patent discusses two specific fibrates, gemfibrozil and bezafibrate, and provides experimental results and a structure for hydroxylated gemfibrozil. However, the '236 provides no structural description of the fibrate genus. U.S. Patent No. 6,680,340 claims a method of lowering triglyceride levels by administering "a thyroid hormone receptor beta agonist in combination with a fibrate." The '340 Patent lists five examples of fibrates, but provides experimental results for fenofibrate only, and provides no structural description of fibrates generally. U.S. Patent No. 6,372,251 claims a composition "consisting essentially of a semi-solid formulation of a fibrate..." The '251 Patent states that fenofibrate "is representative of a broad class of compounds having pharmaceutical utility as lipid regulating agents. More specifically, this compound is part of a lipid-regulating agent class of compounds commonly

known as fibrate..." However, the '251 Patent does not provide any structural description of the fibrate genus.

The above list was identified with a cursory search of the USPTO website, and is not meant to be exhaustive. Applicant realizes that the scope of issued claims in unrelated cases does not constitute binding precedent. However, the cited patents clearly illustrate that the term fibrate is sufficiently well known in the art that a precise structural description is unnecessary to convey the scope of the genus.

The Office Action states that claims 6-10 are rejected for failing to comply with the enablement requirement. According to the Office Action, the skilled artisan cannot predict with any reasonable certainty which fibrates will be effective to treat neoplasms.

Applicant has amended claims 6-10 to recite a method of inhibiting aldose reductase activity in a cell rather than a method of treating a neoplasm. The present application discloses experimental data showing that three different fibrates (bezafibrate, gemfibrozil, and clofibric acid) inhibit aldose reductase activity (see Example 20 and Table 1). This disclosure is sufficient to convince the skilled artisan that fibrates generally are capable of inhibiting aldose reductase activity.

As discussed above with regard to written description, the Office Action acknowledges that "Fibrates are well known in the art as lipoprotein lipase activators and hypolipidemic drugs." Indeed, the art regularly refers to fibrates as a class having these characteristics. For example, Scatena et al. states "Fibric acid derivatives are well-known antihyperlipoproteinemias drugs..." (Scatena et al., page 781, right column, first full paragraph).

Given the well known shared characteristics of fibrates, the skilled artisan would recognize that experimental data showing the ability of three different fibrates to inhibit aldose reductase activity would be sufficient to generalize this activity to fibrates as well. A similar situation is seen in Scatena et al., which discloses experimental results showing that three specific fibrates (bezafibrate, gemfibrozil, and clofibric acid) induce differentiation in human myeloid leukemia (Scatena et al., Abstract). From these results, Scatena et al. conclude "this study does confirm the differentiating activity of fibric acid derivatives" (Scatena et al., page 785, right column, second full paragraph). This reference illustrates the ability of skilled artisans to make general conclusions about fibrates as a class based on experimental results for a few species. Given the understanding in the art that fibrates share a set of functional traits, the disclosure in the present application of experimental data showing that three specific fibrates inhibit aldose reductase is sufficient to enable the skilled artisan to inhibit aldose reductase activity using fibrates generally.

Rejections under 35 U.S.C. 102:

The Office Action states that claims 6-10 are rejected as being anticipated by Hirst et al. (Radiother Oncol 15:55), claims 6-9 are rejected as being anticipated by Scatena et al. (Cell Death Differ 6:781), claims 6 and 8-10 are rejected as being anticipated by Calais et al. (Radiother Oncol 22:99), claims 6 and 8-10 are rejected as being anticipated by Cohen et al. (Clin Invest 71:74), and claims 6-7 and 9 are rejected as being anticipated by Kawamura et al. (Anticancer Res 19:4099).

Applicant has amended claims 6-10 to recite a method of inhibiting aldose reductase activity in a cell rather than a method of treating a neoplasm. The Office

Action acknowledges that the ability to inhibit aldose reductase constitutes a "previously unknown mechanism of action" (Office Action, page 11). Since none of the cited references disclose the ability of fibrates to inhibit aldose reductase, the references do not anticipate the claims as currently amended.

CONCLUSION

In view of the foregoing, it is submitted that all remaining claims are in condition for allowance. Accordingly, Applicants respectfully request that a Notice of Allowance be issued. If Applicants can do anything more to expedite this application, Applicants request that the Examiner contact the undersigned at (310) 788-3218.

Respectfully submitted,
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